



## UNITED STATES DEPARTMENT OF COMMERCE

Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

08/586594			
APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

19/004 594 01/10/98 10/10/98

EXAMINER

ART UNIT PAPER NUMBER

RECEIVED

JAN 09 1998

KLAUBER &amp; JACKSON

DATE MAILED:

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

- ☐ Responsive to communication(s) filed on the Election of 9-8-97
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

- ☒ Claim(s) 1-66 is/are pending in the application.
- Of the above, claim(s) 13-62, 64-65 is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 1-12, 63, 66 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☒ Claim(s) 1-66 are subject to restriction or election requirement.

## Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

DOCKETED CFI

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

TO SEPARATE, H. TOP AND BOTTOM EDGES, SNAP-APART AND TARD CARBON

FORM PTO-892 (REV. 2-92)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		SERIAL NO. 00586594	GROUP/ART UNIT 1812	ATTACHMENT TO PAPER NUMBER 12			
NOTICE OF REFERENCES CITED				APPLICANT(S) Friedman et al.					
U.S. PATENT DOCUMENTS									
		DOCUMENT NO.	DATE	NAME	CLASS	FILING DATE IF APPROPRIATE			
A	5	623748	7/77	Friedman et al.	435	11/31/91			
B									
C									
D									
E									
F									
G									
H									
I									
J									
K									
FOREIGN PATENT DOCUMENTS									
		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG.	PP. SPEC.
L	2	725425	7/97	WO/US	Friedman et al.				
M	3	712037	4/97	WO/US	Friedman et al.				
N	9	719952	11/97	WO/US	Friedman et al.				
O	9	635989	11/96	WO/US	Friedman et al.				
P									
Q									
OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)									
R		Friedman et al. Nature Medicine 2(5) 1996 p 585-89							
S		Friedman et al. Nature Medicine 6(9) 1996 p 1170-80							
T		Friedman et al. Cell 84 1996 p 491-95							
U		Friedman et al. Science 271 1996 p 990-96							
V		Friedman et al. Cell 83 1995 p 1563-71							
W									
X									
Y									
Z									
AA									
AB									
AC									
AD									
AE									
AF									
AG									
AH									
AI									
AJ									
AK									
AL									
AM									
AN									
AO									
AP									
AQ									
AR									
AS									
AT									
AU									
AV									
AW									
AX									
AY									
AZ									
BA									
BB									
BC									
BD									
BE									
BF									
BG									
BH									
BI									
BJ									
BK									
BL									
BM									
BN									
BO									
BP									
BQ									
BR									
BS									
BT									
BU									
BV									
BW									
BX									
BY									
BZ									
CA									
CB									
CC									
CD									
CE									
CF									
CG									
CH									
CI									
CJ									
CK									
CL									
CM									
CN									
CO									
CP									
CQ									
CR									
CS									
CT									
CU									
CV									
CW									
CX									
CY									
CZ									
DA									
DB									
DC									
DD									
DE									
DF									
DG									
DH									
DI									
DJ									
DK									
DL									
DM									
DN									
DO									
DP									
DQ									
DR									
DS									
DT									
DU									
DV									
DW									
DX									
DY									
DZ									
EA									
EB									
EC									
ED									
EE									
EF									
EG									
EH									
EI									
EJ									
EK									
EL									
EM									
EN									
EO									
EP									
EQ									
ER									
ES									
ET									
EU									
EV									
EW									
EX									
EY									
EZ									
FA									
FB									
FC									
FD									
FE									
FF									
FG									
FH									
FI									
FJ									
FK									
FL									
FM									
FN									
FO									
FP									
FQ									
FR									
FS									
FT									
FU									
FV									
FW									
FX									
FY									
FZ									
GA									
GB									
GC									
GD									
GE									
GF									
GG									
GH									
GI									
GJ									
GK									
GL									
GM									
GN									
GO									
GP									
GQ									
GR									
GS									
GT									
GU									
GV									
GW									
GX									
GY									
GZ									
HA									
HB									
HC									
HD									
HE									
HF									
HG									
HH									
HI									
HJ									
HK									
HL									
HM									
HN									
HO									
HP									
HQ									
HR									
HS									
HT									
HU									
HV									
HW									
HX									
HY									
HZ									
IA									
IB									
IC									
ID									
IE									
IF									
IG									
IH									
II									
IJ									
IK									
IL									
IM									
IN									
IO									
IP									
IQ									
IR									
IS									
IT									
IU									
IV									
IW									
IX									
IY									
IZ									
JA									
JB									
JC									
JD									
JE									
JF									
JG									
JH									
JI									
JJ									
JK									
JL									
JM									
JN									
JO									
JP									
IQ									
IR									
IS									
IT									
IU									
IV									
IW									
IX									
IY									
IZ									
KA									
KB									
KC									
KD									
KE									
KF									
KG									
KH									
KI									
KJ									
KK									
KL									
KM									
KN									
KO									
KP									
KQ									
KR									
KS									
KT									
KU									
KV									
KW									
KX									
KY									
KZ									
LA									
LB									
LC									
LD									
LE									
LF									
LG									
LH									
LI									
LJ									
LK									
LL									
LM									
LN									
LO									
LP									
LQ									
LR									
LS									
LT									
LU									
LV									
LW									
LX									
LY									
LZ									
MA									
MB									
MC									
MD									
ME									
MF									
MG									
MH									
MI									
MJ									
MK									
ML									
MM									
MN									
MO									
MP									
MQ									
MR									
MS									
MT									
MU									
MV									
MW									
MX									
MY									
MZ									
NA									
NB									
NC									
ND									
NE									
NF									
NG									
NH									
NI									
NJ									
NK									
NL									
NM									
NN									
NO									
NP									
NQ									
NR									
NS									
NT									
NU									
NV									
NW									
NX									
NY									
NZ									
OA									
OB									
OC									
OD									
OE									
OF									
OG									
OH									
OI									
OJ									
OK									
OL									
OM									
ON									
OO									
OP									
OQ									
OR									
OS									
OT									
OU									
OV									
OW									
OX									
OY									
OZ									

081586594

Attachment 12

The drawings submitted with this application were declared informal by the applicant. Accordingly they have not been reviewed by a draftsman at this time. When formal drawings are submitted, the draftsman will perform a review.

Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Serial Number: 08/586591

Page 2

Art Unit: 1812

### DETAILED ACTION

1. Applicant's election with traverse of GROUP I, claims 1-14, 63 AND 66 in Paper No. 11 OF 9-4-97 is acknowledged. The traversal is on the ground(s) that the proteins and mutations of Group I, as well as the nucleic acids (NA) and fragments would be of interest for the various applications related to the development of assays using the receptor, and that the protein of Group I are related to the NA and fragment. This is not found persuasive because the exact nature of the statement to establish or support a traversal is not clear. However, it would appear that applicants are of the position that the various groups are related and should therefore be examined together. This is not persuasive because "relatedness" is not a proper basis for holding the restriction to be improper. Applicants have not presented sufficient reasons to show that the restriction is in error. But the examiner has met all of the criteria for holding the restriction to be proper, because independent and/or distinctness was shown, and it would certainly pose a serious burden on the examiner to both search and examine each of the inventive groups-particularly since the groups encompass several variant forms of the Ob-R, as well as modified/alter forms of these different variants. The fact that the groups may be related and that there is possible overlap in some of the searches is not sufficient for holding the restriction to be improper-particularly as the searches in the electronic commercial data bases do not necessarily overlap.

The requirement is still deemed proper and is therefore made FINAL.

It is also pointed out that the written restriction also required an election of specie if certain inventive group(s) was elected. This was particularly relevant for Group I, claim 14, but applicants election failed to include an election of specie. However, upon reconsideration the election of specie requirement for the mutations is **withdrawn**, and all of the claimed mutants will be examined herein. Given the scope of these various mutations, to further request that the examiner rejoin all the groups and examine them together would be much more than a serious burden. Accordingly, this office action is directed to the merits of Group I, claims 1-14 63 and 66.

Serial Number: 08/586591

Page 3

Art Unit: 1812

2. The disclosure is objected to because of the following informalities:

At page 19, line 8 "inerspecies" is misspelled.

At page 19, lines 17-18 it is stated that the NA are of Seq ID No 1-5, but from the actual sequence listing the NA are Seq ID No's 1, 3, 5, 7, & 9. Likewise, at line 24 it is stated that the AA are of Seq ID No 6-10, but from the actual sequence listing the NA are Seq ID No's 2, 4, 6, 8, & 10.

For clarity, "the" should appear before "group" at line 2 of claim 2.

At page 25-26 the specification is not clear in defining Ob-Ra, OB-Rb and OB-Re. At lines 28-31 the statement that the OB-Ra "N-terminus diverges from published OB-R sequence upstream of Cys 88" appears to be in contradiction with other portions of the specification and Fig 2B. The statement that the OB-Rb "N-terminal portion appears to be truncated, diverging from the published OB-R sequence upstream of Pro 664" appears to be in contradiction with other portions of the specification and Fig 2B. The statement that the OB-Re "corresponds to published OB-R to His 796, where it diverges." appears to be in contradiction with other portions of the specification and Fig 2B.

Appropriate correction is required.

3. Claims 5-7, 9, 11 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite and confusing for failing to clearly define what is intended by Box 1 or 2. At page 8, Fig 2, page 18 and 25 of the specification, reference is made to Box 1 and Box 2, but it is not clear what this represents, nor is there a definition for such. Further, the repeated recitation of Box 1 and Box 2 does not appear to be necessary at lines 7-8 of the specification and claim 11. At page 15, Fig 2 refers to Box 1 and Box 2, but it is not clear if these are the same boxes. The nature of what is encompassed by this should be defined at its first occurrence in the specification.

Serial Number: 08/586591

Page 4

Art Unit: 1812

Claim 6 is indefinite for failing to clearly define the C-terminal. Does applicants mean the very last amino acid residue or certain portions of the C-terminal? Further, at page 7-8 it appears that applicants intend the c-terminal of murine Ob, but page 9 refers to splice variants.

Claims 7a, 7b, 9b, 9c and 14 are indefinite, incomplete and confusing for failing to recite a point of reference for the sequence and residue numbers referred to therein. This is further confusing and contradictory from the specification which defines this in different way relative to human or murine OB-R; nor is it always exactly clear which variant form of the Ob-R this numbering represents, thus, it is not clear what the controlling meaning is for the claim interpretation. This is further complicated by the fact that the specification uses variant to mean different things throughout the specification, such as for splice variants, naturally occurring variant, or variant that are the direct result of specific modifications. The claims should clearly have a point of reference for the numbering intended, such as by a specific Seq Id No, or with reference to a mature/native, which particular specie form (e.g. human or mouse form), wherein the form/variant/length is clearly identified. Furthermore, claims 6g and 9b refer to just "OB-R", and it is not clear which specific Ob-receptor is intended by this designation. At page 17 of the specification, applicants define the various alphabetical designation by reference to italics, and capitals, but at page 25 "OB-R" is defined as splice forms. Yet at page 20 "OB-R" is defined in terms of Tartaglia's publication, but it is not clear if applicants intend for this to be the human or mouse form, which are not totally identical, and wherein both have a minimum of 889 amino acid residues. Applicants should amend the specification and claims to recite consistent terminology without introducing new matter.

Claims 5-6, 9 and any claim that refers to the OB receptor by the designations of OB-Ra, OB-Rb, OB-Rc, OB-Rd OB-Re are also indefinite and confusing and contradictory for failing to be consistent in their meaning. At certain pages of the specification (pg 6) these variant receptors are defined by Seq Id No's 2, 4, 6, 8, & 10, but at other places they are defined as in Fig 2b, which is also different from the definition at page 86 wherein these designation are defined in

Serial Number: 08/586591

Page 5

Art Unit: 1812

terms of their C-terminal sequences of Seq Id No's 11-----> 15. This is further confusing because Fig 2b list the following amino acids past the L.S. @ 889 as 5, 273, 3, and 11 for OB-Ra, OB-Rb, OB-Rc and OB-Rd, but according to the actual Seq ID (No 11--->14), the number of residues are 8, 276, 7 and 14 respectively. This is similar for OB-Re, which according to Fig 2b has 9 residues after His @ 796, but the Seq Id (No 15) list 11 residues. Clarification/correction is requested without the introduction of new matter.

4. Claims s 1-14, 63 & 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain variant forms of the OB-R, does not reasonably provide enablement for: a) Ob-R devoid of characterization as in claims 1, 5, 8, 9a, 9b, 10-13, 63 & 66; b) for Ob-R with limited characterization, or merely defined by abbreviations as in claims 2 and 5; c) for any Ob-R merely defined by the primers of claims 3-4; and d) for any and all variant OB-R as in claims 5, 6g, 7 and 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

These various issues will be addressed herein below because the specification does not appear to be enabling for the full scope of the polypeptide of these claims. First of all it is pointed out that the Examiner concedes that the specification has provided enablement for making some of the claimed products, but there is insufficient examples, evidence or guidance to enable all of the claimed Ob-R polypeptide. While it is well settled that a specification need not contain examples in order to be enabling, in the express absence of such, the specification must provide enablement alternatively in the form of evidence or guidance. It is also known and accepted that examples, evidence of guidance are not required if, on its face, it is clear to the skilled artisan that the claims are enabled; and when there is no reason to question the objective truths of applicant's mere statement of assertions that the full scope of the claimed ob polypeptide are enabled by the specification's teachings. The following are reasons for questioning the objective truth.

Serial Number: 08/586591

Page 6

Art Unit: 1812

Relative to issue "a" and "b", the claims are non-enabling for a protein that is merely referred to by a name, or very limited characterization as in claim 2 without the recitation of any other identifying or fingerprinting characteristic-physically or functionally. For instance, claim 1 refers to the receptor by a name, but fails to set forth any physical characteristics (MW and how it is determined, the amino acid composition or sequence, pI, or other fingerprinting characteristics), or specific or non-specific functional/biological activity, nor does it require a homogeneous or purified protein. A name or an abbreviation is arbitrarily assigned by the researcher who isolates or discovers the protein based on the activity they have associated with it, however, as is the case with most proteins, there are generally many activities associated with a protein, and any one scientist will assign a name to a protein based on the particular activity that they are researching. This often leads to confusion in the art about what protein is actually being referred to as compared to other proteins with the same physical features, and it also results in any one protein being given/assigned different or multiple names, even though the resulting protein per se is the same despite the various names assigned to it. This is especially true for new and novel proteins, because names are subject to change, as has been the case for many proteins, especially for many of the cytokines. In fact the abbreviation the Ob-r protein is also referred to as leptin-receptor. Therefore, a name, without any identifying characteristics, as with claim 1 which does not even recite any functional characteristics, does not serve to sufficiently distinguish or define the features of a protein so as to enable the skilled artisan to know what is encompassed and intended by such in order to practice the claimed invention. This is further complicated by the fact that there are often multiple or variant forms of a protein, such that without specifically define characteristics, the skilled artisan would not know how to obtain the proper protein. The failure of the claim specifically claim the receptor by characterizing in the instant case is further complicated by the fact that the art has shown that there are multiple forms of the OB-R, which the size of these variant forms differ drastically, despite some homology in a large portion of the receptor at the extracellular, transmembrane and intracellular domains. In a similar manner,



Serial Number: 08/586591

Page 7

Art Unit: 1812

claims 3-4 are not enabled for the full scope of Ob-r that can be identified by the small primer sequences. These claims read on variant forms as well as modified forms of the receptor.

The claims are also non-enabling for failing to define the point of reference of the numbering of the amino acid residues, and therefore, are not enabled for all OB-r the have the designated number of residues. By merely referring to the number of amino acids that the protein has without specifying to nature or make-up of these specific amino acid, the claims read on any ob-r protein that is the result of any or all possible insertions, substitutions, and deletions as long as the resulting protein has the designated number of c- and n-terminal residues; and this also reads on fusion protein and conjugates for which there is no enablement. However, the specification is not enabled form such, and the skilled artisan would encounter undue experimentation for trying to determine the make-up of the protein that would have this wide range of amino acid residues-especially in the absence of the claims to recite biological activity.

Relative to issue "c" as briefly discussed above and issue "d", there is no broad based enablement for generating the various potential OB-R variants, particularly since the claims do not require that the variants possess a specific "biological activity". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, absent a sufficient number of examples; or evidence or sufficient guidance; or in the absence of a reproducible and/or predictable functional assay; or in the absence of concrete structure/function studies to guide the skilled artisan to amino acid residues or regions where such modification could be made on the ob-r protein with reasonable assurance that the resulting analogs will possess the desired activity. The following is an overview of information provided in the specification that applicants appear to be relying upon to enable the breadth of the claims. The specification at page 29 refers to analogs of the Ob polypeptide that result from substitutions (preferably with Ala or conservative substitutions) and possibly deletions at the divergent/non-conservative sites between the mouse and human protein. Further, these substitutions refer to a comparison between the human and

Serial Number: 08/586591

Page 8

Art Unit: 1812

mouse forms of the protein, but the claims are not limited to these two specie forms, thus, it is not clear how such divergence and modification are determined when other specie forms are involved (e.g. is the other specie form compared to human or mouse in order to determined divergent sites for possible modification). Applicants simply state that the modifications can be made and the resulting analog can be tested to determine its activity. There are no binding studies to determine binding sites which represent potential sites for modification to obtain both agonist and antagonist. Without binding studies, the skilled artisan would be faced with undue experimentation for trying to determine if a particular analog or variants possessed the same binding specificity to the receptor as the mature/native protein. The generation of any type of modification to produce the various variants and analogs and the testing of the effect that the modification produces may not be considered undue experimentation if there is some guidance, in the absence of sufficient examples, that limits the specific location and type of modifications, as well as involves a routine screening procedure. See *Ex parte Mark* 12 USPQ 2d 1904 (Bd. Of Pat. App. and Inter. 1989). In this regard, not only is there not sufficient examples to enable the breadth of the claims, but the guidance give is also not sufficient because all that applicants have provided is mere sequence information about the protein and limited biological activity studies, and places where there is divergence between the human and mouse sequences. There are no teachings for where biologically active regions are (such as functional activity, binding activity, epitopic regions, stability regions etc.); nor information about the tertiary or quaternary structure of the protein, and page 8 merely refers to antigenic fragments and derivatives (also at pg 28-30 and 34-37).

While it is conceivable that conservative substitutions do not materially affect the structure and function of a protein, this is not always true. It would, however, appear that the specification may be enabled for conservative substitutions (pg 8), but the claims are not limited to such, but instead encompass agonist as well as antagonist, but the is insufficient guidance for obtaining receptor variants that possess the full scope of the modification of the claims. There is no

Serial Number: 08/586591

Page 9

Art Unit: 1812

guidance given as to the composition of the various variants and analogs that would function as a ob-r protein as broadly claimed, and no assay taught for screening the functioning analogs from the non-functioning analogs. The claims are not enabled by the specification as filed because they embraces an undeterminable number of embodiments and variations which are not directly supported by the specification and testable in a screening assay. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structural/functional relationship, e.g. such as various sites or regions where the biological activity resides or regions directly involved in binding, stability, or catalysis; and in providing the correct three-dimensional spatial orientation for biologically active or binding sites, or for sites which represent other characteristics/properties of the protein. These or other regions may also be critical determinants of antigenicity. These various regions can tolerate only relatively conservative substitutions or no substitutions, however, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions, insertions or deletions), and the nature and extent of the changes that can be made in these positions in order to obtain the various ob analogs. Such a definition might also read on previously characterized proteins, or alternatively, might include proteins with additional functions or activities neither envisioned nor enabled by applicants in the current invention. See *Ex parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986) with regard to the issue raised above and *In re Fisher*, 166 USPQ 18.

There are no specific teachings for what kind or the nature or extent of what the specific substitutions, deletions or additions would have to be in order for the resulting protein to have the

Serial Number: 08/586591

Page 10

Art Unit: 1812

same activity as the ob-r protein. And although the claims state that the protein must have the recited property, in the absence of the specification to teach and enable structure/function studies on the protein, the skilled artisan would have the resort to a substantial amount of undue experimentation in order to determine which amino acids would be substituted, added or deleted while still maintaining the desired biological activity. Further, the cited portion of the specification only provide "boiler-plate" citations for modification on proteins in general, but has not shown how to specifically extrapolate this to ob, therefore, this constitute inadequate guidance for the vast number of analogs/mutants that are encompassed by the claims, and is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The scope of applicant's claims encompass modification on the protein that would be critical as well as non-critical for the biological activity of the protein. Thus, even if critical residues were identified, which in this case they are not, the mere identification of these critical regions would not be sufficient as the ordinary artisan would immediately recognize that the modified site must assume the proper three-dimensional configuration to be active-which conformation is dependent upon surrounding residues. The substitution/insertion/ deletion of non-essential residues can often destroy activity, therefore, it is deemed that to make each of the possible amino acid modifications for each of the non-essential residues, even if only conservative replacements were made, would also constitute undue experimentation. The introduction of non-conservative substitution, non-naturally occurring amino acids, deletions or insertions further raises the possible number of species. Therefore, Applicants have not presented enablement commensurate in scope with the claims.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

Serial Number: 08/586591

Page 11

Art Unit: 1812

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-14, 63 & 66 are rejected under 35 U.S.C. 102(a) or (e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tartaglia et al or Snodgrass et al (748).

No one claim is specifically directed to a single form of the Ob-R. In fact claims 1, 5, 8-13 and 63 and 66 define the receptor merely by a name(s); claims 2 and 5 merely define the receptor by limited characterization or abbreviations; claim 3-4 merely define the receptor by primers used to clone the encoded protein; and claims 6-7 and 9 define the receptor by N or C-terminal residues which are encompassed by the amino acid residues of each of the following prior art. In view of the broad manner in which the claims are written, each of the prior art anticipate most of the claims or anticipate portions of the alternative limitations of the claims.

Tartaglia et al disclose the cloning of the human and mouse OB-R (pg 1264-1267) The nucleic acid and amino acid sequence for both human and mouse OB-R has been compared (see Fig 8) and both contain the WSX motif consistent with other Class I cytokine receptors (Pg 1265,

Serial Number: 08/586591

Page 12

Art Unit: 1812

1267). The mouse Ob-R has 894 amino acid, and the human form is much longer with 1165 residues, and at page 1267, it is taught that the human and mouse OB-R are 78% identical. Both receptors have long extracellular domain, and a short transmembrane and short intracellular domain. The intracellular domain of human and mouse OB-R is conserved up to the last five amino acids consistent with mouse OB-R at residue 889 (pg 1265 and 1267). While not other variant forms were expressly disclose, at several places throughout the citation, there is reference to the possible existence of other splice variants (see pg 1266, 1267, 1268 and 1269). Also taught is that the cloning of this receptor will provide understanding in the mechanism of leptin action and provides important implications for understanding body weight dysfunctions and the treatment/regulation of such (pages 1268-1269). In view of the fact that it has been well established that many cytokines have multiple forms of the receptor as well as variant of some of the forms of the receptors (this is especially true for many cytokines and the hematopoietins), the teachings at 1266, 1267, 1268 and 1269 for the existence of splice variants provide clear motivation for the skilled artisan to use the DNA to probe a genomic library to obtain variant forms of the receptor (See Ex parte Anderson, 30 USPQ d. 1867)-thus, rendering obvious the instant claims that recite a DNA sequence that is different from that disclosed in the prior art.

Snodgrass et al disclose a novel hematopoietin receptor having a WSX motif and having sequence homology to other hematopoietin receptors such as the Il-6R, wherein this receptor was detected in various human tissue. The receptor of Snodgrass et al is now known as one form of the Ob/leptin receptor (see the claims). The detection of two different sizes of mRNAs suggested the presence of homologous genes or alternative splicing (col 15). At col 2. Lines 57-59, and col 10 it is taught that this receptor can be used to screen for a ligand; further taught is that the receptor can be used to cause cellular proliferation or differentiation (col 13), additionally taught at col 12-14 is the preparation and use of antisense an ribozymes for use to inhibit translation of the receptor and the use of the DNA to diagnose for disease resulting from aberrant expression of the receptor; and that the receptor can be used for the production of antibodies, agonist and

Serial Number: 08/586591

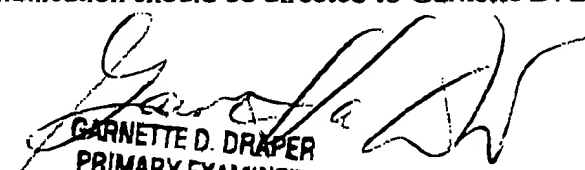
Page 13

Art Unit: 1812

antagonist (col 6 & 10). At col 5 it is taught that altered forms of the DNA can be prepared and used; and that the receptor can be expressed using various prokaryotic and eukaryotic cells with the aid of various regulatory sequences (col 6-10). Further taught at col 5 lines 34-45 and at col 10 is that the receptor can be ligated to heterologous sequences to produce fusion protein or chimeric proteins, in which the receptor can be fused to an antibody. While Snodgrass et al did not expressly disclose the identity of the ligand as the ob/leptin protein or that their receptor was one form of the ob/leptin receptor, in view of the fact that the receptor has been identified as a hematopoietin receptor and in view of the fact that the instant receptor has a WSX motif and belongs to the family of hematopoietin receptors, despite the difference in what the receptor is referred to by their different names, the receptor protein per se and the DNA encoding it would appear to be the same and is therefore anticipated by the art [See In re Best, 195 USPQ 430, and In re Swinehart, 169 USPQ 226)] and the burden is upon applicants to establish a patentable difference. As stated above, although the prior art does not refer to their receptor as the ob/leptin receptor, and does not expressly teach alternative or variant forms, at col 4, line 20-23 it is stated that multiple libraries may have to be screened for a full length cDNA. In view of the fact that it has been well established that many cytokines have multiple forms of the receptor as well as variant of some of the forms of the receptors (this is especially true for many cytokines and the hematopoietins), the teachings at col 15 in conjunction with the teachings at col 4 lines 19-39 provide clear motivation for the skilled artisan to use the DNA to probe a genomic library to obtain variant forms of the receptor (See Ex parte Anderson, 30 USPQ d. 1867)-thus, rendering obvious the instant claims that recite a DNA sequence that is different from that disclosed in the prior art.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The other prior art listed on the 892 is cited as of interest to show related art.

8. Any inquiry concerning this communication should be directed to Garnette D. Draper at telephone number (703) 308-4232.

  
GARNETTE D. DRAPER  
PRIMARY EXAMINER  
GROUP 1800